REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining in this application be allowed.

Amendments

The specification was amended to correct several grammatical/inadvertent errors.

Claims 20-32 were subject to a restriction requirement as being directed to a method which is independent and distinct from the previously presented and examined Claims 16-19. Accordingly, Claims 20-32 were canceled without prejudice or disclaimer. Applicants reserve the right to file a divisional application directed to these claims.

These amendments have been made in accordance with 37 C.F.R. §1.121 as amended on November 7, 2000. As required, attached hereto is an appendix illustrating the changes made to the specification and Claims 16 and 17.

In view of the above, Claims 16-19 are now in this application.

Rejection Under 35 U.S.C. §112, first paragraph

Claims 17-19 stand rejected under 35 U.S.C. §112, first paragraph. Without acquiescing in this rejection and solely for the purpose of expediting allowance of otherwise allowable subject matter, Applicants have deleted the objected to language of Claim 17 without prejudice to filing a continuation application directed to this subject matter. Applicants submit that this rejection is now moot.

Rejection Under 35 U.S.C. §102(b)

Claims 16 and 18 stand rejected under 35 U.S.C. §102(b) over Fadok, et al., J. Immunology, 148(7):2207-2216 (1992) ("Fadok"). For the following reasons, this rejection is traversed.

Initially, it is well established law that to anticipate a claim, a single prior art reference must teach, either expressly or inherently, each and every element of the claimed invention. See M.P.E.P. § 2131; Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986).

With regard to the above, now presented Claim 16 recites pharmaceutical compositions comprising human apoptotic bodies or apoptotic cells and a pharmaceutically acceptable excipient. Fadok, on the other hand, merely discloses the generation of mouse apoptotic bodies or cells suspended in RPMI. As such, Fadok cannot anticipate now presented Claim 16 because Fadok simply does not disclose human apoptotic bodies or apoptotic cells let alone pharmaceutical compositions of such cells.

As to the issue of pharmaceutical compositions in general, Applicants take issue with the assertion in the Office Action that the RPMI suspending solution constitutes a pharmaceutically acceptable excipient. As noted at Col. 15, lines 55-65, in U.S. Patent No. 6,482,986 (copy enclosed) recites that RPMI 1640 contains 2% heat-inactivated fetal calf serum, 2 mM L-glutamine, 1 mM sodium pyruvate, 100 UI/ml of penicillin, 100 μg/ml of streptomycin and 15 mM PIPES. Applicants maintain that such a solution does not constitute a pharmaceutically acceptable excipient if for no other reason that fetal calf

serum would likely induce an immunogenic response when introduced, e.g., intravenously into a treated patient.[1]

Accordingly, Fadok does not anticipate Claim 16. Claim 18 is dependent from Claim 16 and to the extent that Claim 16 is not anticipated by Fadok, so too is Claim 18 not anticipated by Fadok. Withdrawal of this rejection is requested.

In view of the above, Applicants submit that this application is now in condition for allowance. A Notice to that effect is earnestly solicited.

Respectfully submitted,

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[1] Intravenous injection constitutes one route of administration contemplated by this invention.

Attachment to Reply and Amendment

Marked-up Copy

The paragraph bridging pages 1 and 2 was amended as follows:

--Two mechanisms of cell death in the body are recognized, necrosis and apoptosis. Apoptosis is the process of programmed cell death, described by Kerr et al in 1992 [Kerr JFR, Wyllie AH, Currie AR (1992). "Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. *"British Journal of Cancer* **26:** 239-257"], by which steady-state levels of the various organ systems and tissues in the body are maintained as continuous cell division and differentiation takes place. Cells undergoing apoptosis often exhibit distinctive morphological changes such as a pronounced decrease in cell volume, modification of the cytoskeletons resulting in pronounced membrane blebbing, a condensation of the chromatin, and degradation of the DNA into oligonucleosomal fragments. Following these morphological changes, an apoptotic cell may break up into a number of small fragments known as apoptotic bodies, consisting essentially of membrane-bound bodies containing intact organelles, chromatin, etc. Apoptotic bodies are normally rapidly removed from the body by phagocytosis by macrophages, dendritic cells and other antigen presenting cells, before they can become lysed and release their potentially pro-inflammatory intracellular contents.

The paragraph at page 3, lines 3-16, was amended as follows:

--Many cells undergoing apoptosis can be identified by a characteristic 'laddering' of DNA seen on agarose gel electrophoresis, resulting from cleavage of DNA into a series of fragments. These changes occur a few hours before death of the cell as defined by the ability of a cell to exclude vital dyes. The appearance of DNA laddering on agarose gel electrophoresis following extraction of DNA from cells is one recognised method of

identification of apoptosis in cells [Loo, D.T. and Rillema, J.R. (1998) "Measurement of Cell Death," *Methods in Cell Biology* **57**: 251-264], although it is not always sensitive enough to detect apoptosis. *In situ* labelling of nuclear DNA fragmentation, for example, using commercially available terminal dUTP nick end labelling (TUNEL) assays, **is** [are] an alternative and more reproducible measure for the determination of fragmented DNA in apoptotic cells and cells undergoing apoptosis [Gavrieli Y, Sherman Y, Ben-Sasson SA (1992)", Identification of programmed cell death in situ via specific labelling of nuclear DNA fragmentation". *Journal of Cell Biology* **119:** 493-501].--

The paragraph bridging pages 8 and 9 was amended as follows:

--Yet another method is the application of oxidative stress to cells extracorporeally (see for example Buttke and Sandstrom (1994) "Oxidative Stress as a Mediator of Apoptosis," Immunology Today, Vol. 15:7-10). This can be achieved by treating the cells, in suspension, with chemical oxidizing agents such as hydrogen peroxide, other peroxides and hydroperoxides, ozone, permanganates, periodates, and the like. Biologically acceptable [such] oxidizing agents are preferably used, so as to reduce potential problems associated with residues and contaminations of the apoptotic cells and apoptotic bodies so formed.--

Claim 16 was amended as follows:

--16. (amended) A pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of human apoptotic bodies and/or apoptotic cells.

Claim 17 was amended as follows:

17. (amended) The pharmaceutical composition of claim 16 [which is suitable for administration to a mammalian patient to treat or to effect prophylaxis against neurodegenerative and other neurological medical disorders] wherein said apoptotic cells and/or bodies comprise no more than 35 weight percent necrotic cells and/or bodies.--